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(51) International Patent Classification 5 : G01N 27/447	A1	(11) International Publication Number: WO 93/06475
		(43) International Publication Date: 1 April 1993 (01.04.93)

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(54) Title: ELECTROPHORESIS WITH CHEMICALLY SUPPRESSED DETECTION

(57) Abstract

Improved capillary electrophoresis apparatus of the type that generally includes a capillary tube, the capillary tube having a sample inlet end and an outlet end, a first electrode in electrical communication with the inlet end of the capillary tube, a second electrode in electrical communication with the outlet end of the capillary tube and a high voltage power supply in electrical communication with the first and second electrodes. The improvement is to connect a miniature Ion Chromatography membrane suppressor to the outlet end of the capillary tube, to connect a conductivity detector to the membrane suppressor and to place the second electrode in the regenerant compartment of the membrane suppressor. The method embodiment of the invention for anion analysis includes the steps of: (a) separating anions of interest by capillary electrophoresis in a buffer solution; (b) exchanging cations of the buffer for regenerant cations using an ion chromatography membrane suppressor to reduce the electrical conductivity of the buffer to produce a suppressed buffer; and (c) measuring the electrical conductivity of the suppressed buffer to determine the separated anions. Similarly, the method embodiment of the invention for cation analysis includes the steps of: (a) separating cations of interest by capillary electrophoresis in a buffer solution; (b) exchanging anions of the buffer for regenerant anions using a stationary means for exchanging anions thereby reducing the electrical conductivity of the buffer to produce a suppressed buffer; and (c) measuring the electrical conductivity of the suppressed buffer to determine the separated cations.

ELECTROPHORESIS WITH CHEMICALLY SUPPRESSED DETECTION

TECHNICAL FIELD

The present invention relates to method and apparatus using capillary electrophoresis and ion suppression for the determination of anions or cations.

BACKGROUND ART

Capillary electrophoresis is a known technique involving electrophoresis in small bore capillaries. This approach provides methods for efficient analytical separations of ionic species including macromolecules.

10 A typical capillary electrophoresis system is shown in Fig. 1. As can be seen, a capillary is positioned between two solvent reservoirs containing electrolyte. Electrodes present in each of the reservoirs and coupled to a power supply capable of delivering upwards to 30 kV

15 per 100 cm of capillary provide a voltage gradient to drive charged species through the capillary bore. A detector is positioned at a point between the two high voltage electrodes to permit detection of various ionic species migrating in the capillary. A detector so

20 positioned is sometimes referred to as an on-column detector.

A number of approaches have been developed to detect the solutes separated by capillary electrophoresis depending, in part, upon the nature of the solute

detected. UV absorption and fluorescence have been the
most commonly used detection modes. Mass spectrometric,
radiometric and electrochemical methods of detection
have also been utilized. With regard to electrochemical
5   detection, amperometry and conductivity methods have
been used.

Off-column amperometric detection utilizing a porous
glass capillary to cover a crack in the capillary has
also been reported. Wallingford, R.A., et al., Anal.
10   Chem. (1987) 59, 1762-1766; Ewing, A.G., et al., Anal.
Chem. (1989) 61, 292A-303A. End-column amperometry and
conductivity detection have also been performed. Huang,
et al., Anal. chem. (1991), 63, 189-192. A significant
problem with on-column and end-column detection
15   utilizing electrochemical techniques is the effect of
the high voltage applied to the electrodes to generate
the voltage gradient across the capillary. Small
variations in this high voltage gradient (typically
ranging from 20-30 kV) have significant impact upon the
20   voltages used for amperometric detection and
conductivity detection which generally utilizes less
than 1 volt in such detection systems.

Even for off-column electrochemical detection, a
significant signal to noise problem exists due to the
25   presence of relatively high concentrations of the
electrolyte needed in the eluent to generate the voltage
gradient across the length of the capillary bore. This
is especially problematic for detection utilizing
conductivity since such measurements are more
30   significantly affected by electrolyte concentration than
amperometric detection which is based primarily upon the
detection of redox reactions at the detection
electrodes.

Although electrolyte suppression has been used primarily
in ion exchange chromatography in conjunction with
conductivity detection (see e.g. U.S. Patent Nos.
3,897,213 3, 3,920,397, 3,925,019, 3,956,559, 4,474,664,
5   4,751,004, 4,459,357 and 4,999,098), such suppressors
have not been adapted for use with capillary
electrophoresis.

The references discussed above are provided solely for
their disclosure prior to the filing date of the present
10   application and nothing herein is to be construed as an
admission that the inventor is not entitled to antedate
such disclosure by virtue of prior invention.

The following is a discussion of the background art
from a different viewpoint. Electrophoresis is a well
developed chemical analysis technique. A review reference
on this subject is Chapter 9 of Chromatography –
Fundamentals and Applications of Chromatographic and
Electrophoretic Methods, Part A: Fundamentals and
Techniques, edited by E. Heftmann, Elsevier Scientific
Publishing Company, 1983, herein fully incorporated by
reference. Capillary electrophoresis (CE) is an important
advance in electrophoresis which was pioneered by Jorgenson
and Lukacs as reported in Analytical Chemistry 1298 (1981)
and in 222 Science 266 (1983), each of which are herein
fully incorporated by reference. Since a small diameter
capillary is used in CE, a relatively high applied voltage
can be used without generating problematic thermal
gradients in the capillary. The efficiency of separation
in CE is a function of, among other things, the applied

voltage. The efficiency of CE is relatively high, e.g., in excess of 400,000 theoretical plates.

5   The following is a description of a typical CE experiment. A 50-100 micrometer internal diameter silica capillary tube is filled with a suitable conducting buffer. The outlet end of the capillary is immersed in a reservoir containing the buffer and an electrode. A sample containing fluorescent ions of interest is introduced into
10   the inlet end of the capillary and then the inlet end of the capillary is placed into another reservoir containing the buffer and another electrode. A voltage of 30,000 volts is impressed between the electrodes. 'A fluorescence detector is positioned near the outlet end of the capillary
15   to detect the ions of interest.

     The movement of the sample ions of interest is controlled by two factors: (1) electrophoretic migration; and (2) electroosmotic flow. Electrophoretic migration is the
20   migration of the ions of interest towards the oppositely charged electrode under the influence of the electric field. Electroosmotic flow is bulk flow of the buffer in the capillary when the inside surface of the capillary which is in contact with the buffer comprises fixed charge
25   sites which in turn have corresponding mobile counter-ions in the buffer. An unmodified silica capillary surface comprises silanol (Si-OH) groups that are negatively charged (Si-O-) when the pH of the buffer is greater than about 2, and positively charged (Si-OH$_2^+$) when the pH of the
30   buffer is less than about 2.

     When the surface is negatively charged, then the corresponding mobile counter-ions of the negatively charged surface, e.g., sodium ions (Na+), migrate under the
35   influence of the electric field and in the process drag the

bulk solvent with them. Thus, the direction of the electroosmotic flow is from the positive to the negative electrode when the surface is negatively charged.

5   When the surface is positively charged, then the corresponding mobile counter-ions of the positively charged surface, e.g., biphosphate ions (HPO_4^{-2}), migrate under the influence of the electric field and in the process drag the bulk solvent with them. Thus the direction of the
10   electroosmotic flow is from the negative to the positive electrode when the surface is positively charged. A positively charged surface can also be obtained, e.g., by adsorbing hydrophobic cations onto the inside surface of the capillary.
15

     When the surface is not charged, then there is no electroosmotic flow. Thus, depending on the charge (positive or negative) of the ions of interest, the nature and extent of capillary surface charging and the polarity
20   of the applied voltage, electroosmosis can augment, counteract or even override the electrophoretic migration. Since sample components to be determined must travel from the inlet end of the capillary to the detector which is located near the outlet end of the capillary, it is
25   essential that they move in the desired direction.

     Waters Chromatography Division of Millipore of Milford, Massachusetts and Dionex Corporation of Sunnyvale, California are the leading domestic manufacturers of CE
30   instruments for the analysis of common ions. The Waters instrument utilizes indirect photometric detection, see for example Jandik et al., LC GC magazine, September 1991 issue, beginning on page 634, herein fully incorporated by reference. The Dionex system uses a photometric detector
35   or a fluorescence detector, see for example the Dionex

advertisement in LC GC magazine, September 1991 issue, on
page 639, herein fully incorporated by reference. At the
present time, the preferred detection method in CE for the
determination of common ions is indirect photometric
5   detection.

    Even though CE has many advantages, it also has several
characteristics that need improvement. For example, the
concentration detection limit of CE could be improved.
10

DISCLOSURE OF INVENTION

    In accordance with the invention, apparatus and methods
15   are provided for increasing the sensitivity of detection
of ionic species separated by capillary electrophoresis.
The apparatus includes capillary electrophoretic
separating means, suppressor means and detector means.
The capillary electrophoretic separator means typically
20   include a small bore capillary having a first end in
communication with a first electrolyte reservoir which
also contains a first electrode means. The capillary
also has a second end having an ion conduction means in
communication with the second electrolyte reservoir
25   containing a second electrode means. The first end of
the capillary is capable of receiving electrolyte from
the first reservoir which is present throughout the
entire bore of the capillary. The ion conducting means
at the second end of the capillary is capable of
30   conducting current generated between the first and
second electrodes when an electrolyte is present in said
capillary and said first and said second reservoirs and
a voltage is applied to the electrodes. This
construction essentially isolates the suppressor means

and detector means from the current and high voltage
gradient generated between the two electrodes.

The suppressor means comprises at least one capillary
effluent compartment having an inlet and an outlet end.
5 The inlet end is in communication with the second end
of the capillary in the capillary electrophoretic
separating means. The suppressor means also contains
at least one regenerant compartment means and at least
one ion exchange member partitioning the capillary
10 effluent compartment means and the regenerant
compartment means. This ion exchange membrane is
permeable to ions of the same charge (i.e., positive or
negative) as the counter ion of the ionic species to be
separated and impermeable to ions of the same charge as
15 the ionic species to be separated.

The detector means of the apparatus is in communication
with the outlet end of the suppressor means and is
suitable for detecting resolved ionic species eluting
therefrom.

20 In operation, the ionic species of the sample are
separated in the bore of the capillary of the
electrophoretic separating means by a voltage gradient
generated by applying a voltage across the electrodes.
The effluent from this separating means flows into the
25 suppressor means and in particular the capillary
effluent compartment means. The regenerant compartment
means contains a regenerant which is dissociated into
cations and anions. Since the ion exchange membrane
partitioning the capillary effluent compartment and
30 regenerant compartment is preferably permeable to ions
of the same charge (i.e., positive or negative) as the
counter ions of the ionic species to be detected, such
counter ions are capable of crossing the membrane into
the regenerant compartment. The regenerant ion of the

same charge is capable of crossing the membrane from the
regenerant compartment into the effluent in the
capillary effluent compartment. The net effect is to
exchange the counter ion of the ionic species of
5   interest.

For example, if an anion is to be detected and the
electrolyte is sodium hydroxide, a typical regenerant
is sulfuric acid. For each molecule of electrolyte one
sodium ion is replaced with a hydronium ion from the
10 regenerant sulfuric acid to form water. Similarly, the
sodium ion associated with the anionic species of
interest is replaced with a hydronium ion from the
regenerant solution. As a consequence, the overall
conductivity of the eluent decreases and the overall
15 conductivity of ionic species and counter ion increases.
The thus treated effluent then flows to a detector.
Since the overall concentration of electrolyte has been
reduced, the sensitivity of detecting conductivity
increases.

The following is a disclosure of the invention from a
different viewpoint. The instant invention is the
provision of suppressed detection for CE. A primary
benefit of the instant invention is improved limits of
detection. One apparatus embodiment of the invention is an
improved capillary electrophoresis apparatus of the type
that generally includes a capillary, the capillary having a
sample inlet portion and an outlet portion, a first elec-
trode in electrical communication with the inlet portion of
the capillary, a second electrode in electrical communi-
cation with the outlet portion of the capillary and a power
supply in electrical communication with the first and
second electrodes. The improvement comprises means for
exchanging ions, the means for exchanging ions being in
liquid communication with the capillary, the means for
exchanging ions being stationary.

Another apparatus embodiment of the invention is an
improved capillary electrophoresis apparatus of the type
that generally includes a capillary, the capillary having a
sample inlet portion and an outlet portion, a porous
conduit means, the channel of the porous conduit means
being in liquid communication with the capillary, a first

electrode in electrical communication with the inlet
portion of the capillary tube, a second electrode in
electrical communication with the porous conduit means, a
power supply in electrical communication with the first and
5   second electrodes. The improvement comprises means for
exchanging ions, the means for exchanging ions being in
liquid communication with the channel of the porous conduit
means, the means for exchanging ions being stationary.

10   One method embodiment of the invention is an
electrophoresis anion analysis method comprising the steps
of: (a) separating anions of interest by electrophoresis
in a buffer solution; (b) exchanging cations of the buffer
for regenerant cations using a stationary means for
15 exchanging cations thereby reducing the electrical conduc-
tivity of the buffer to produce a suppressed buffer; and
(c) measuring the electrical conductivity of the suppressed
buffer to determine the separated anions.

20   Another method embodiment of the invention is an
electrophoresis cation analysis method comprising the steps
of: (a) separating cations of interest by electrophoresis
in a buffer solution; (b) exchanging anions of the buffer
for regenerant anions using a stationary means for
25 exchanging anions thereby reducing the electrical
conductivity of the buffer to produce a suppressed buffer;
and (c) measuring the electrical conductivity of the
suppressed buffer to determine the separated cations.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic diagram of a prior art apparatus for performing capillary electrophoresis derived from Fig. 1 of Ewing, et al., _Anal. Chem._ (1989), _61_, 292A-303A.

Fig. 2 is a schematic diagram of one of the embodiments of the invention.

Fig. 3 is a schematic diagram of the ion conducting means and suppressor means used in Example 1.

Fig. 4 is an electropherogram demonstrating the separation and detection of various anionic species by measuring conductivity using an embodiment of the invention.

Fig. 1A is a schematic drawing of one apparatus embodiment of the invention;

Fig. 2A is a cross-sectional side view of one suppressor embodiment of the invention;

Fig. 3A is a cross-sectional side view of one electrical conductivity cell embodiment of the invention;

Fig. 4A is a cross-sectional side view of another electrical conductivity cell embodiment of the invention;

Fig. 5A is a schematic drawing of another apparatus embodiment of the invention;

Fig. 6A is a cross-sectional side view of one buffer bridge embodiment of the invention.

MODES FOR CARRYING OUT THE INVENTION

The system of the present invention is useful for
determining a large number of solutes so long as such
solutes are anions or cations. A suitable sample
5   includes surface waters and other liquids such as
industrial chemical wastes, body fluids, beverages such
as fruits and wines and drinking water. When the term
"ionic species" is used herein, it includes species in
ionic form and components of molecules which are
10   ionizable under the conditions of the present system.

Generally, the ionic species which are particularly
susceptible to detection by the apparatus and methods
disclosed herein are those species that absorb visible
or ultraviolet light only weakly and therefore are
15   poorly detected by photometric absorbance detection.
Examples of weakly absorbing species are common
inorganic ions such as chloride, sulfate, sodium and
potassium as well as many organic species such as
acetate, succinate and trimethylamine.

20   As used herein, a "capillary electrophoretic separating
means" refers to any means for separating ionic species
which contains an elongate narrow bore through which an
electrolyte can be passed and which has ends that can
be placed in contact with first and second electrolyte
25   reservoirs. Although in the preferred embodiments,
typical narrow bore capillaries generally used in prior
art devices are used, the term "capillary" is not
limited to such capillaries. Rather, as used herein
capillary refers to any elongate bore in a solid support
30   having the dimensions on the order of magnitude of the
internal dimensions of prior art capillary devices.
Such capillaries have acceptable bore diameters ranging
from 1 to 1000 μm, more preferably 25 to 100 μm.
Generally, the length of such capillaries are about 1
35   cm to 10 meters, more preferably 20 cm to 100 cm. Based

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on these parameters, capillaries for use in practicing
the present invention may comprise such capillaries or
may comprise channels of irregular or regular shape
formed in a solid support such as silica by etching or
5   machining. In some instances it may be desired to form
one side of a capillary in two separate blocks of solid
support material which can thereafter be joined to form
the complete capillary. In general, the cross-sectional
area of such non-standard capillaries is substantially
10   similar to that of conventional capillaries.

Referring to Fig. 2, a simplified apparatus for
performing the present invention is illustrated. The
system includes capillary 10 which contains a first end
12 immersed in an electrolyte reservoir 14. Also
15   contained within this reservoir is first electrode 16
and an electrolyte 18. This first electrode 16 is
connected to high voltage supply unit 20. The second
end of the capillary 10 has an ion conduction means 22
attached thereto. This ion conduction means can be any
20   conducting device that allows conduction of the current
resulting from the high voltage current generated
between electrodes 16 and 24 through capillary 10. Such
conducting means, because of the use of suppressor means
and detector downstream from the ion conduction means,
25   requires that this ion conduction means be chosen such
that a substantial amount of the mass flow through
capillary 10 pass by ion conduction means 22 toward
suppressor tube 34. One embodiment of conductive means
comprises a gap between the capillaries with an
30   insulating sleeve having one or more conducting holes.
Alternatively, the insultaing sleeve may be loosly
fitting to form an eluent gap between the capillaries
and the sleeve. A further embodiment of the ion
conduction means includes a capillary gap with a porous
35   sleeve capable of conducting ions through the pores
contained therein. Such gaps, pores or holes are used

to provide a channel for ionic current between the
eluent at the second end of capillary 10 and the second
electrode 24 and should be chosen such that at least
about 50% of the mass flow passes such conducting means

5   to remain in the downstream mass flow channel 26. In
general, the nature of such gaps, holes or pores should
be large enough to provide sufficient ionic current to
complete the high voltage circuit but not be so large
as to allow the eluent to be diverted into reservoir 30.

10   In the preferred embodiments, the ion conductivity means
22 is an amphoteric membrane, preferably a sleeve which
is capable of engaging the second end of capillary 10
and an end of downstream conduit 28. A specific method
for producing such an amphoteric membrane sleeve is

15   disclosed in Example 1. Other methods will be readily
apparent to those skilled in the art and basically
involve derivitizing a membrane with both anionic and
cationic functional groups.

The second reservoir 30 also contains an electrolyte 32

20   which is in contact with the second electrode 24 and the
ionic conduction means 22 to complete the high voltage
circuit. As a consequence, the voltage drop along the
remaining flow path to the detector is negligible.

In general, the electrolyte present in at least the

25   first reservoir and the capillary bore is dependent upon
the ionic species to be detected. When the ionic
species is an anion, the electrolyte is preferably the
salt form of a weak acid. Examples include sodium
borate, sodium carbonate and sodium hydorxide. When the

30   ionic species to be detected is a cation, the
electrolyte is preferably the salt form of a weak base.
An example of such an electrolyte is hydrogen chloride.

An important aspect of practicing the invention, however, involves the proper choice of voltage to be applied across the electrophoresis electrodes 16 and 24. Since a high voltage circuit is produced between

5   electrode 16 and electrode 24 via the ionic conducting means 22 and electrolyte solution 32, there is no voltage potential downstream from ionic conducting means 22 to drive the ionic species and the electrolyte into the suppressor means. To overcome this problem, the

10 voltage is chosen such that it induces an electroendosmotic flow in the direction from the first reservoir to the detector. Electroendosmotic flow is generated primarily because of a local voltage which exists at the interface between the inside surface of

15 the capillary and the electrolyte solution. This potential, sometimes referred to as the zeta potential, is dependent upon the material forming the inside surface of the capillary and the solution in contact with this surface.

20 In a silica capillary the charge on the inside wall of the capillary is negative and the direction of electroendosmotic flow is toward the negative electrode or away from the positive electrode. It is possible to reverse the direction of electroendosmotic flow by

25 coating or derivatizing the wall of the silica capillary such that the charge on the wall is positive instead of negative. Under such circumstances to ensure electroendosmotic flow to the detector, the polarity of the electrode in the first reservoir should be reversed.

30 It is also possible to use capillaries made of materials such as polyethylene or polystyrene that have no surface charge. These materials can then be functionalized to generate a positive or negative charge for example by quanternization or sulfonation respectively using known

35 chemistries. The major reason for controlling electroendosmotic flow is to control separation

resolution of the ionic species being separated. If the
electroendosmotic flow is the same direction as the
electrophoretic direction of the ionic species the
separation resolution is less than when the
5   electroendosmotic flow is in the opposite direction of
the electrophoretic direction.

The downstream connector 28 is connected to a suppressor
tube 34 contained in a regenerant compartment 36. The
regenerant compartment 36 contains a regenerant 38
10   appropriate for the ionic species to be detected and the
electrolyte used for capillary electrophoresis.

The suppressor tube 34 has an internal bore which forms
a compartment to contain the effluent from the capillary
10.   The inlet portion of this capillary effluent
15   compartment is connected to downstream conduit means 28.
An ion exchange membrane is positioned between this
capillary effluent and the regenerant compartment. In
general, suppressor tube 34 comprises an ion exchange
membrane to facilitate ionic transport between the
20   capillary effluent compartment and the regenerant
compartment. The ion exchange membrane is chosen such
that it is preferentially permeable to the counter ion
of the ionic species. Thus, if the ionic species is an
anion its counter ion is a cation. The ion exchange
25   membrane is chosen to be permeable to cations. The
converse is also true. Such tubular membranes can be
purchased commercially such as the cation exchange
membrane tube Nafion® available from Perma Pure
Products, Toms River, N.J. It is to be understood,
30   however, that the suppressor means need not be a tubular
form of an ion exchange membrane. Alternate embodiments
include flat membranes such as that disclosed in U. S.
Patent No. 4,999,098 incorporated herein by reference.

Although it is preferable that the cross-sectional area
of the downstream conduit 28 be the same as that of the
cross-sectional area of the bore of capillary 10 and
further that the cross-sectional area of the capillary

5 effluent compartment 34 have substantially the same
cross-sectional area, it is not necessary that such
cross-sectional areas be the same. Useful results have
been obtained where the inside diameter of the circular
bore capillary 10 was 75 microns and the inside diameter

10 of the Nafion® cation exchange membrane tube was 400
microns. However, these results can be further improved
when a 350 μm diameter plug is inserted inside the
Nafion® tube to reduce the effective cross-sectional
flow area of the ion suppressor (see Example 1).

15 The suppressor length should be suffiecient to exchange
cations or anions in the effluent but not be so long as
to result in substantial band broadening. Such
suppressor length can be from 100 μm to 10 cm,
preferably 1 mm to 1 cm.

20 The foregoing describes a passive diffusion suppressor
means for reducing electrolyte concentration. However,
any suppressor system can be used in practicing the
invention including those utilizing the application of
electrical fields across the ion exchange membrane to

25 increase the rate of ion exchange above that which would
otherwise be obtained by diffusion limited exchange
kinetics. See e.g. U.S. Patent No. 4,999,098
incorporated herein by reference.

After passing the ion exchange membrane, the thus

30 treated effluent is substantially depleted in the
electrolyte and counter ions to the ionic species of
interest. Such treated effluent may be directed to a
flow through conductivity cell for detection of the
ionic species present. Alternatively, one or both of

the detection electrodes 42 and 44 can be inserted into
the treated effluent stream exiting the suppressor
means.   When used in this manner, the outlet of the
suppressor means may be maintained in the regenerant
5   solution 38 provided the electrodes are positioned
sufficiently within this end region so that conductivity
is not adversely influenced by diffusion of regenerant
ions into the effluent stream. In general, when one or
more of the electrodes are inserted into the suppressor
10   means outlet, the linear flow rate of the effluent
should be sufficient to offset the potential diffusion ·
of the regenerant ions into the effluent stream which
would otherwise defeat the purpose of the suppressor
means.

15   Although the foregoing has described the invention
primarily within the context of open-tube capillary zone
electrophoresis, it is believed that other modes of
capillary electrophoresis may be practiced using the
invention. Such other modes include isotachophoresis,
20   micellar electrokinetic capillary chromatography,
capillary gel electrophoresis and isoelectric focusing.

The following sets forth a specific embodiment of the
invention and is not to be construed as a limitation of
the claims as appended hereto.

25   Example 1

Referring to Fig. 3, the separation capillary 10 was a
fused silica capillary with dimensions of 75 μm i.d.,
375 μm o.d., and 75 cm length. It was butted up against
a second fused silica capillary 28 of the same i.d. and
30   o.d. but about 6 mm long.

The amphoteric ion exchange membrane tube 22 with dimensions of about 400 μm i.d., 800 μm o.d., and about 1 cm long also acted as a sleeve to hold the two pieces of capillary 10 and 28 together. The amphoteric

5   membrane sleeve was attached to the capillaries by tightly tying nylon monofilament (75 μm diameter) around the sleeve. The amphoteric membrane sleeve was made from a substrate tube made of polyethylene/polyvinyl acetate. This tube (Microline®) was obtained from

10   Thermal Plastic Scientific, Warren, N.J. It was radiation grafted with vinylbenzylchloride (VBC) to about 50% VBC by weight. The grafted tube was refluxed for 14 hours in a 1 M solution of dimethylamino-acetonitrile in methanol and allowed to cool for 6

15   hours. Following rinses in methanol and water, the tube was heated to about 60°C in 1 M sodium hydroxide solution for 90 minutes. This reaction hydrolyzes the $-CN$ to $-CO_2^-$. The resulting tube contains the following functional group covalently bonded to the VBC molecules

20   in the membrane: $-N^+(CH_3)_2CH_2CO_2^-$.

The other end of capillary 28 was inserted into a length of Nafion® cation exchange tubing with approximate dimensions of 400 μm i.d., 800 μm o.d., and 1 cm long (Perma Pure Products, Toms River, N.J.) which served as

25   the suppressor 34. The suppressor was held onto capillary 28 by tying with Nylon monofilament. Much of the internal volume of the suppressor was taken up with a 350 μm o.d. by 5 mm long plug made from capillary with the ends sealed with epoxy resin. The approximate

30   length of the suppressor from the exit of tube 28 to the detector electrode 44 was 6 mm.

One of the detector electrodes 44 was made by inserting a 127 μm platinum wire into a 150 μm i.d., 350 μm o.d. by 2 cm long capillary and filling the remaining volume

35   with epoxy resin. The face of the capillary was

polished to expose the end of the platinum wire. This
electrode was inserted about 1 mm inside the suppressor,
and the other end of the wire was connected to the
conductivity detector cables.   The second detector
5   electrode 42 was placed into the regenerant solution 38.

The electrolyte in both the first electrolyte reservoir
and in the second electrolyte reservoir was a 10 mM
borax solution, pH 9.1. The regenerant 38 was a 15 mM
sulfuric acid solution.

10   The applied high-voltage was 20 kV, which resulted in
a current of 20.5 μA.   A 5 second electrophoretic
injection was used to inject a sample of 20 μM each of
the   following   anions: quinate,   benzoate,
benzenesulfonate,   acetate,   phthalate,   phosphate,
15   formate, and fluoride. The results are shown in Fig. 4.

The following modes for carrying out the invention are
from a different viewpoint. Referring now to Fig. 1A,
therein is shown a schematic drawing of an apparatus
embodiment of the invention including a fused silica
capillary 10a. The inlet portion of the capillary 10a is
shown immersed in a buffer 11a contained in a first buffer
reservoir 12a. The buffer 11a is usually water based but
can be based on other solvents such as alcohols,
acetonitrile, tetrahydrofuran and glycols. A power supply
13a supplies a selected voltage (or current) to a first
electrode 14a via a wire 15a. A sample to be analyzed 16
is contained in a sample reservoir 17a. The sample to be
analyzed 16a contains ions of interest. The outlet portion
of the capillary 10a is connected to a suppressor 18a. The
high voltage power supply 13a is connected to the
suppressor 18a via a wire 19a. A regenerant 20a is
contained in a regenerant reservoir 21a. A tube 22a
connects the reservoir 21a with the suppressor 18a. The
regenerant 21a flows through the suppressor 18a, through a

tube 23a to waste. As will be discussed below in detail,
the suppressor 18a contains an ion exchange material or
means and the regenerant is used to regenerate this ion
exchange material or means. A tube 24a connects the
suppressor 18a to an electrical conductivity detector 25a.
A tube 26a connects the conductivity detector 25a to an
optional additional detector 27a such as an optical or an
electrochemical detector. A tube 28a is shown immersed in
buffer 11a contained in a second buffer reservoir 29a and
5   connected to the detector 27a. The tube 28a is preferably
of a relatively large internal diameter for the reasons to
be discussed below. An aliquot of the sample 16a can be
introduced into the inlet portion of the capillary 1a0 by
lifting the inlet portion of the capillary 10a from the
10 reservoir 12a temporarily placing it in the sample
reservoir 17a and then placing it back into the reservoir
12a. This can be done manually but preferably it is done
by automated means as is well known in the art. The volume
of sample 16a so introduced into the inlet portion of the
15 capillary 10a, of course, depends on the length of time the
inlet portion of the capillary 10a is immersed into the
sample 16a because the level of the sample 16a is higher
than the level of the buffer 11a in the second buffer
reservoir 29a. Alternatively, the sample 16a can be
20 introduced into the inlet portion of the capillary 10a by
electrophoretic migration and/or electroosmotic flow, and
it should also be possible to use a sample injection valve.
The fused silica capillary 10a is preferred in the
invention because of its excellent thermal conductivity
25 characteristics as is well known in the art. However, such
a capillary is not critical in the invention and the
capillary 10a can be made almost any material.
Furthermore, although the capillary 10a is preferably
circular in cross section, this is not critical either. A
30 single capillary 10a is preferred in the invention but this
is also not critical. Thus, the capillary of the
invention, in its broadest scope, is a conduit as defined
below. The inlet portion of the capillary of the invention

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is that portion where the sample to be analyzed is
introduced. The outlet portion of the capillary of the
invention is that portion where electrophoretic zones leave
the capillary and enter, e.g., the suppressor. Normally,
the inlet portion of the capillary and the outlet portion
of the capillary are the opposite ends of the capillary.
5   However, this is not critical in the invention. Thus, for
example, it is contemplated in the invention that a sample
can be introduced into the middle of a capillary with its
cations of interest migrating toward one end of the
capillary while its anions of interest migrate toward the
10   other end of the capillary.

     Referring now to Fig. 2A, therein is shown a detailed
cross-sectional view of the suppressor 18a. A tubular
jacket 30a, made for example of silicone rubber or
15   plasticized polyvinyl chloride, surrounds a length of
tubing 31a made of NAFION™ sulfonated fluoropolymer ion
exchange material. The outlet portion of the capillary 10a
is shown inserted into one end of the of the tubing 31a.
The tubing 24a is shown inserted into the other end of the
20   tubing 31a. A miniature tee 32a is shown inserted into one
end of the jacket 30a. Another miniature tee 33a is shown
inserted into the other end of the jacket 30a. The
capillary 10a is sealed in the tee 33a by sealant 34a such
as room temperature vulcanizing silicone rubber. The
25   capillary tube 24a is sealed in the tee 32a by sealant 35a
such as room temperature vulcanizing silicone rubber. A
platinum wire 19a is shown inserted through the jacket 30a
and the end of the wire 19a within the jacket 30a is the
second electrode 36a. The electrode 36a can,
30   alternatively, be embedded into the tubing 31a but
preferably it is positioned exterior of the tubing 31a. In
some cases, the electrode 36a is better positioned near the
end of the tube 31a where it is connected to the capillary
10a. Obviously, the electrode can be positioned in the
35   reservoir 21a.

The internal diameter of the tubing 31a preferably is
about the same as the internal diameter of the capillary
10a. Such small bore ion exchange material is not

5 commercially available. The smallest internal diameter
NAFION™ tubing has an internal diameter of about 400
micrometers. However, the internal diameter of such
material can be made smaller by a number of techniques such
as: (a) by swelling the NAFION™ tubing in alcohol and then

10 stretching it; (b) heating the NAFION™ tubing and then
stretching it; (c) a combination of (a) and (b); (d) making
a small internal diameter tube of NAFION™ by dipping a
small diameter wire, e.g. a 75 micrometer tungsten wire, in
a colloidial dispersion of NAFION™, thermally curing the

15 NAFION™ deposited on the wire and then withdrawing the wire
from the so formed NAFION™ tube (United States Patent
4,731,263 to Grot, herein fully incorporated by reference,
discloses making colloidial dispersions of NAFION™ as does
Martin in Analytical Chemistry 1639 (1982), herein fully

20 incorporated by reference); and preferably by (e) drilling
or piercing a small hole through a solid piece of swelled
ion exchange material followed by drying to shrink it onto
the capillary 10a and the tubing 24a.

25 A conduit is herein defined as any structure having at
least one channel therethrough. The tubing 31a is one
example of a conduit comprising ion exchange material.
However, the invention is not limited to a conduit in the
shape of a tube. For example, the conduit can be in the

30 shape of a perforated mass of ion exchange material, e.g.,
a perforated bead of conventional ion exchange resin such
as DOWEX™ 50W or DOWEX™ 2 ion exchange resin (DOWEX™ is a
trademark of The Dow Chemical Company). A sheet of ion
exchange material can be used in a conduit of the

35 invention, e.g., by clamping it between plates having

suitable channels and openings. The conduit of the
invention preferably comprises an ion exchange material
that extends from the channel to the exterior of the
conduit. However, the invention will also work when the

5   conduit comprises merely a material that conducts ions or
can be made to conduct ions such as cellulose acetate
membrane or even porous glass. A porous conduit can be
imbibed with a liquid ion exchanger as discussed below.

10   Referring now to Fig. 3A, therein is shown a detailed
cross-sectional view of one embodiment of a cell of the
electrical conductivity detector 25a. The cell includes a
short piece of flexible tubing 36b having a suitably small
internal diameter, e.g., 125 micrometers. A fine platinum

15   wire 37a is shown piercing the tubing 36b. Another fine
platinum wire 38a is also shown piercing the tubing 36a.
The wires 37a and 38a can be so positioned by first
piercing the tubing 36b with a fine hypodermic needle,
e.g., a 30 gauge hypodermic needle, inserting the platinum

20   wire into the hypodermic needle and then withdrawing the
hypodermic needle while holding the platinum wire in place.
The wires 37a and 38a are positioned as close together as
possible without touching, e.g., a spacing of 100-300
micrometers. The wires 37a and 38a are the conductivity

25   detector electrodes and are, of course, connected to the
electronics portion of a suitable electrical conductivity
detector such as an Ion Chromatography electrical
conductivity detector.

30   Referring now to Fig. 4A, therein is shown a detailed
cross-sectional view of another embodiment of a cell of the
electrical conductivity detector 25a. The cell includes a
short piece of flexible tubing 39a having a suitably small
internal diameter, e.g., 125 micrometers. A stainless

35   steel wire 40a is shown piercing the tubing 39a. Another

stainless steel wire 41a is shown piercing the tubing 39a
on the opposite side of the tubing 39a. The ends of the
wires 40a and 41a are positioned close together in the tube
39a without touching, e.g., a spacing of 100 micrometers.

5 The wires 40a and 41a are the conductivity detector
electrodes and are, of course, connected to the electronics
portion of a suitable electrical conductivity detector such
as an Ion Chromatography electrical conductivity detector.

10 Preferably, the resistance to flow of the elements in
line after the outlet of the capillary 10a are exceedingly
low so as to maintain the flat-fronted flow profile in the
capillary 10a. Since this ideal is not perfectly attained,
it is advantageous to slightly elevate the buffer level in

15 the reservoir 12a relative to the buffer level in the
reservoir 29a.

Referring now to Fig. 5A, therein is shown a schematic
drawing of another apparatus embodiment of the invention

20 which is similar to the embodiment shown in Fig. 1A. The
elements shown in Fig. 5A that are the same as the elements
shown in Fig. 1A have the same reference numerals.
However, it will noticed that in Fig. 5A the wire 19a is no
longer directed to the suppressor 18a. Instead, the wire

25 19a is directed to a buffer bridge 42a. The buffer 11a is
also contained by a third buffer reservoir 43a. A tube 44a
connects the reservoir 43a with the buffer bridge 42a. The
buffer 11a in the reservoir 43a flows through the buffer
bridge 42a, through a tube 45a and then to waste. As will

30 be discussed below in detail, the buffer bridge 42a
contains a porous material or other means such as simply a
fractured capillary tube (ala Linharcs and Kissinger,
Analytical Chemistry 2076 (1991), herein fully incorporated
by reference) which provides electrical communication

35 between the buffer within the buffer bridge and the buffer

within or exiting the outlet portion of the capillary 10a.
The buffer bridge is connected to the suppressor 18a by
tubing 46a.

5   Referring now to Fig. 6A, therein is shown a detailed
cross-sectional view of the buffer bridge 42a. The buffer
bridge 42a is similar in most respects to the suppressor
18a as will be appreciated by comparing Fig. 6A with Fig.
2A. A tubular jacket 47a, made for example of silicone
10 rubber or plasticized polyvinyl chloride, surrounds a
length of tube made of a porous material such as porous
glass. The outlet portion of the capillary 10a is shown
inserted into one end of the of the tube 48a. The tubing
46a is shown inserted into the other end of the tube 48a.
15 A miniature tee 49a is shown inserted into one end of the
jacket 47a. Another miniature tee 50a is shown inserted
into the other end of the jacket 47a. The capillary 10a is
sealed in the tee 50a by sealant 51a such as room
temperature vulcanizing silicone rubber. The capillary
20 tube 46a is sealed in the tee 49a by sealant 52a such as
room temperature vulcanizing silicone rubber. A platinum
wire 19a is shown inserted through the jacket 47a and the
end of the wire 19a within the jacket 47a is the second
electrode 36a. The electrode 36a can, alternatively, be
25 embedded into the tubing 48a but preferably it is
positioned exterior of the tubing 48a. Obviously, the
electrode 36a can be positioned in the reservoir 43a. It
will be appreciated that the buffer bridge 42a is similar
to the salt bridge of Wallingford and Ewing except that the
30 salt solution (potassium chloride) is being replaced with,
e.g., buffer of a suitable concentration or a solution of
large ions that can not cross the porous barrier. The
tubes 46a, 24a and 26a of Fig. 5A as well as the tubes 24a
and 26a of Fig. 1A are preferably as short as possible
35 because the flow profile in these tubes is generally

parabolic as opposed to the flat-fronted flow profile in
the capillary 10a.

Means for exchanging ions is defined herein as any
5 means which accepts a cation and in return gives up a
cation, any means which accepts an anion and in return
gives up an anion and any means which absorbs salts (such
as the free base form of DOWEX™ 4 ion exchange resin which
absorbs, e.g., copper nitrate from solution, or such as a
10 crown ether which absorbs salt from solution) including a
solid ion exchange material and a liquid ion exchange
material. A stationary means for exchanging ions includes
the suppressor 18a but also would include a device like the
buffer bridge 42a wherein a liquid ion exchanger is
15 positioned within the jacket 47a even though the liquid ion
exchanger can be flowed through the device in place of the
buffer, i.e., even though the liquid ion exchanger is
moving the device is not. Similarly, the porous tube 48a
can be imbibed with a liquid ion exchanger and regenerant
20 can be flowed through the device in place of the buffer. A
tube containing ion exchange resin is a stationary means
for exchanging ions. On the other hand, introducing a
suspension of ion exchange particles into the effluent
buffer from the capillary tube of a CE system before the
25 buffer flows through a conductivity detector (ala Gjerde
and Senson, European Patent Application No. 89110394.7,
publication No. 0 345 782 A2, herein fully incorporated by
reference) is a mobile means for exchanging ions, i.e., the
ion exchange particles move in and with the buffer. Thus,
30 another way of distinguishing the means for exchanging ions
of the invention is that the means for exchanging ions of
the invention is "non-invasive". A non-invasive means for
exchanging ions is a means that is not introduced into the
buffer stream, i.e., a means that is not completely
35 surrounded by the buffer stream, and which preferably

partitions the buffer stream from a separate source of
regeneration cations or anions.

5   A method embodiment of the invention, with respect to
anion analysis, can be understood by reference to Fig. 5A.
The capillary tube 10a is temporarily immersed in the
sample 16a to introduce the sample 16a into the capillary
tube 10a. The sample contains anions of interest. The
buffer 11a contains a salt of a weak acid such as a borate
10   buffer. The ion exchange material of the suppressor 18a is
a cation exchanger such a NAFION™ brand ion exchange
material from DuPont. The regenerant 20a is a source of
hydrogen ions such as dilute sulfuric acid or a suspension
of ion exchange particles in the hydrogen ion form. The
15   power supply 13a is turned on so that the electric field
extends from the buffer bridge 42a and along the bore of
the capillary 10a. If the capillary 10a is negatively
charged as discussed above, then the electrode 14a is made
positive and the electrode 36a is made negative so that the
20   electroosmotic flow is toward the cation exchange material
of the suppressor 18a. In addition, if the capillary 10a
is negatively charged, then the anions of interest tend to
migrate out of the inlet portion of the capillary 10a and
into the reservoir 12a. This tendency is overcome for many
25   anions of interest by the more rapid electroosmotic flow
toward the suppressor 18a. If the capillary 10a is
positively charged as discussed above, then the electrode
14a is made negative and the electrode 36a is made positive
so that the electroosmotic flow is toward the cation
30   exchange material of the suppressor 18a. In addition, if
the capillary 10a is positively charged, then the anions of
interest tend to migrate in the same direction as the
electroosmotic flow, i.e., toward the suppressor 18a.
Thus, there is a distinct benefit in using a positively
35   charged capillary tube 10a in this embodiment. However,

this is not critical and there are benefits from using a
negatively charged capillary tube 10a in this embodiment.
In the suppressor 18a, referring now also to Fig. 2A, the
cations of the buffer are exchanged for hydrogen ions at
5   the inside surface of the ion exchange tube 31a so that the
buffer 11a is converted into a weak acid solution to form a
suppressed buffer solution. This suppressed buffer
solution then flows through the electrical conductivity
detector 25a. The conductivity of the suppressed buffer,
10 as determined by the detector 25a, is relatively low
compared to the conductivity of the buffer 11a. When the
ions of interest flow through the detector 25a, they are
sensitively detected upon the background of the suppressed
buffer. In this respect, the invention is similar to
15 suppressed detection in Ion Chromatography. Hopefully, of
course, the ions of interest are resolved into detected
separate zones by the prior electrophoresis in the
capillary tube 10a. The ion exchange material of the
suppressor 18a is regenerated by the flow of dilute
20 sulfuric acid regenerant 20a flowing around the exterior of
the tube 31a. In the above discussion, the buffer
comprised a salt of a weak acid. However the invention is
not limited to a buffer comprising a salt of a weak acid,
e.g, a strong base can be used such as sodium hydroxide
25 which is converted to water by the suppressor. The buffer,
when a conductivity detector is used and when its cations
are exchanged for the regenerant cations, must be converted
to a solution that has reduced electrical conductivity. In
this respect, a reference to the suppressed detection Ion
30 Chromatography art will indicate other buffers and
regenerant cations that can be used in the invention. The
buffer, when another detector is used than a conductivity
detector and when its cations are exchanged for the
regenerant cations, must be converted to a solution that
35 has a reduced detector response. Most preferably, the

anion of the buffer has about the same electrophoretic
mobility as the anions of interest.

5   Another method embodiment of the invention, with
respect to anion analysis, can be understood by reference
to Fig. 1A and Fig. 2A. The capillary tube 10a is
temporarily immersed in the sample 16a to introduce the
sample 16a into the capillary tube 10a. The sample
contains anions of interest. The buffer 11a contains a
10   salt of a weak acid such as a borate buffer. The ion
exchange material of the suppressor 18a is a cation
exchanger such a NAFION™ ion exchange material from DuPont.
The regenerant 20a is a source of hydrogen ions such as
dilute sulfuric acid or a suspension of ion exchange
15   particles in the hydrogen ion form. The power supply 13a
is turned on so that the electric field extends across the
ion exchange tube 31a and along the bore of the capillary
10a. If the capillary 10a is negatively charged as
discussed above, then the electrode 14a is made positive
20   and the electrode 36a is made negative so that the
electroosmotic flow is toward the cation exchange material
of the suppressor 18a. In addition, if the capillary 10a
is negatively charged, then the anions of interest tend to
migrate out of the inlet portion of the capillary 10a and
25   into the reservoir 12a. This tendency is overcome for many
anions of interest by the more rapid electroosmotic flow
toward the suppressor 18a. If the capillary 10a is
positively charged as discussed above, then the electrode
14a is made negative and the electrode 36a is made positive
30   so that the electroosmotic flow is toward the cation
exchange material of the suppressor 18a. In addition, if
the capillary 10a is positively charged, then the anions of
interest tend to migrate in the same direction as the
electroosmotic flow, i.e., toward the suppressor 18a.
35   Thus, there is a distinct benefit in using a positively

charged capillary tube 10a in this embodiment. However,
this is not critical and there are benefits from using a
negatively charged capillary tube 10a in this embodiment.
In the suppressor 18a the cations of the buffer are
5   exchanged for hydrogen ions at the inside surface of the
ion exchange tube 31a so that the buffer 11a is converted
into a weak acid solution to form a suppressed buffer
solution. If the electrode 36a is negatively charged, then
the effectiveness of the suppressor is enhanced. The
10 suppressed buffer solution then flows through the
electrical conductivity detector 25a. The conductivity of
the suppressed buffer, as determined by the detector 25a,
is relatively low compared to the conductivity of the
buffer 11a. When the ions if interest flow through the
15 detector 25a, they are sensitively detected upon the
background of the suppressed buffer. In this respect, the
invention is similar to suppressed detection in Ion
Chromatography. Hopefully, of course, the ions of interest
are resolved into detected separate zones by the prior
20 electrophoresis in the capillary tube 10a. The ion
exchange material of the suppressor 18a is regenerated by
the flow of dilute sulfuric acid regenerant 20a flowing
around the exterior of the tube 31a. The method embodiment
for anion analysis discussed above in reference to Fig. 1A
25 is preferred over the method embodiment for anion analysis
discussed above in reference to Fig. 5A as being simpler
and probably more effective. In the above discussion, the
buffer comprised a salt of a weak acid. However the
invention is not limited to a buffer comprising a salt of a
30 weak acid, e.g, a strong base can be used such as sodium
hydroxide which is converted to water by the suppressor.
The buffer, when a conductivity detector is used and when
its cations are exchanged for the regenerant cations, must
be converted to a solution that has reduced electrical
35 conductivity. In this respect, a reference to the

suppressed detection Ion Chromatography art will indicate
other buffers and regenerant cations that can be used in
the invention. The buffer, when another detector is used
than a conductivity detector and when its cations are
5   exchanged for the regenerant cations, must be converted to
a solution that has a reduced detector response. Most
preferably, the anion of the buffer has about the same
electrophoretic mobility as the anions of interest.

10   A method embodiment of the invention, with respect to
cation analysis, can be understood by reference to Fig. 5A.
The capillary tube 10a is temporarily immersed in the
sample 16a to introduce the sample 16 into the capillary
tube 10a. The sample contains cations of interest. The
15   buffer 11a contains a salt of a weak base such as a
solution aniline hydrochloride or a salt of a zwitterionic
compound such as glycinium hydrochloride. The ion exchange
material of the suppressor 18a is an anion exchanger such
as DOWEX™ 2 brand ion exchange material from Dow. The
20   regenerant 20a is a source of hydroxide ions such as dilute
sodium hydroxide or a suspension of ion exchange particles
in the hydroxide ion form. The power supply 13a is turned
on so that the electric field extends from the buffer
bridge 42a and along the bore of the capillary 10a. If the
25   capillary 10a is positively charged as discussed above,
then the electrode 14a is negative and the electrode 36a is
positive so that the electroosmotic flow is toward the
anion exchange material of the suppressor 18a. In
addition, if the capillary 10a is positively charged, then
30   the cations of interest tend to migrate out of the inlet
portion of the capillary 10a and into the reservoir 12a.
This tendency is overcome for many cations of interest by
the more rapid electroosmotic flow toward the suppressor
18a. If the capillary 10a is negatively charged as
35   discussed above, then the electrode 14a is positive and the

electrode 36a is negative so that the electroosmotic flow
is toward the anion exchange material of the suppressor
18a. In addition, if the capillary 10a is negatively
charged, then the anions of interest tend to migrate in the
5   same direction as the electroosmotic flow, i.e., toward the
suppressor 18a. Thus, there is a distinct benefit in using
a negatively charged capillary tube 10a in this embodiment.
However, this is not critical and there are benefits from
using a positively charged capillary tube 10a in this
10   embodiment. In the suppressor 18a, referring now also to
Fig. 2A, the anions of the buffer are exchanged for
hydroxide ions at the inside surface of the ion exchange
tube 31a so that the buffer 11a is converted into a weak
base solution to form a suppressed buffer solution. This
15   suppressed buffer solution then flows through the elec-
trical conductivity detector 25a. The conductivity of the
suppressed buffer, as determined by the detector 25a, is
relatively low compared to the conductivity of the buffer
11a. When the cations if interest flow through the
20   detector 25a, they are sensitively detected upon the
background of the suppressed buffer. In this respect, the
invention is similar to suppressed detection in Ion
Chromatography. Hopefully, of course, the cations of
interest are resolved into detected separate zones by the
25   prior electrophoresis in the capillary tube 10a. The ion
exchange material of the suppressor 18a is regenerated by
the flow of dilute sodium hydroxide regenerant 20a flowing
around the exterior of the tube 31a. In the above
discussion, the buffer comprised a salt of a weak base.
30   However the invention is not limited to a buffer comprising
a salt of a weak base, e.g, a strong acid can be used such
as sulfuric acid which is converted to water by the
suppressor. The buffer, when a conductivity detector is
used and when its anions are exchanged for the regenerant
35   anions, must be converted to a solution that has reduced

electrical conductivity. In this respect, a reference to the suppressed detection Ion Chromatography art will indicate other buffers and regenerant cations that can be used in the invention. The buffer, when another detector
5 is used than a conductivity detector and when its anions are exchanged for the regenerant anions, must be converted to a solution that has a reduced detector response. Most preferably, the cation of the buffer has about the same electrophoretic mobility as the cations of interest.
10

Another method embodiment of the invention, with respect to cation analysis, can be understood by reference to Fig. 1A and Fig. 2A. The capillary tube 10a is temporarily immersed in the sample 16a to introduce the
15 sample 16a into the capillary tube 10a. The sample contains cations of interest. The buffer 11a contains a salt of a weak base such as a solution aniline hydrochloride or a salt of a zwitterionic compound such as glycinium hydrochloride. The ion exchange material of the
20 suppressor 18a is an anion exchanger such as DOWEX™ 2 brand ion exchange material from Dow. The regenerant 20a is a source of hydroxide ions such as dilute sodium hydroxide or a suspension of ion exchange particles in the hydroxide ion form. The power supply 13a is turned on so that the
25 electric field extends across the ion exchange tube 31a and along the bore of the capillary 10a. If the capillary 10a is positively charged as discussed above, then the electrode 14a is negative and the electrode 36a is positive so that the electroosmotic flow is toward the anion
30 exchange material of the suppressor 18a. In addition, if the capillary 10a is positively charged, then the cations of interest tend to migrate out of the inlet portion of the capillary 10a and into the reservoir 12a. This tendency is overcome for many anions of interest by the more rapid
35 electroosmotic flow toward the suppressor 18a. If the

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capillary 10a is negatively charged as discussed above,
then the electrode 14a is positive and the electrode 36a is
negative so that the electroosmotic flow is toward the
anion exchange material of the suppressor 18a. In
5   addition, if the capillary 10a is negatively charged, then
the anions of interest tend to migrate in the same
direction as the electroosmotic flow, i.e., toward the
suppressor 18a. Thus, there is a distinct benefit in using
a negatively charged capillary tube 10a in this embodiment.
10 However, this is not critical and there are benefits from
using a positively charged capillary tube 10a in this
embodiment. In the suppressor 18a the anions of the buffer
are exchanged for hydroxide ions at the inside surface of
the ion exchange tube 31a so that the buffer 11a is
15 converted into a weak base solution to form a suppressed
buffer solution. If the electrode 36a is positively
charged, then the effectiveness of the suppressor is
enhanced. The suppressed buffer solution then flows
through the electrical conductivity detector 25a. The
20 conductivity of the suppressed buffer, as determined by the
detector 25a, is relatively low compared to the
conductivity of the buffer 11a. When the cations if
interest flow through the detector 25a, they are
sensitively detected upon the background of the suppressed
25 buffer. In this respect, the invention is similar to
suppressed detection in Ion Chromatography. Hopefully, of
course, the cations of interest are resolved into detected
separate zones by the prior electrophoresis in the capil-
lary tube 10a. The ion exchange material of the suppressor
30 18a is regenerated by the flow of dilute sodium hydroxide
regenerant 20a flowing around the exterior of the tube 31a.
The method embodiment for cation analysis discussed above
in reference to Fig. 1A is preferred over the method
embodiment for cation analysis discussed above in reference
35 to Fig. 5A as being simpler and probably more effective.

In the above discussion, the buffer comprised a salt of a weak base. However the invention is not limited to a buffer comprising a salt of a weak base, e.g, a strong acid can be used such as sulfuric acid which is converted to

5 water by the suppressor. The buffer, when a conductivity detector is used and when its anions are exchanged for the regenerant anions, must be converted to a solution that has reduced electrical conductivity. In this respect, a reference to the suppressed detection Ion Chromatography

10 art will indicate other buffers and regenerant cations that can be used in the invention. The buffer, when another detector is used than a conductivity detector and when its anions are exchanged for the regenerant anions, must be converted to a solution that has a reduced detector

15 response. Most preferably, the cation of the buffer has about the same electrophoretic mobility as the cations of interest.

If a neutral capillary is used, then there is no

20 electroosmotic flow in the capillary. If there is no electroosmotic flow in the capillary, then there is no means of transporting the separated ions to the detector. This problem is overcome in the invention, e.g., by introducing a flowing stream of buffer, water or solvent

25 into the outlet portion of the capillary. Referring now to Fig. 5A, a tee is placed between the outlet portion of the capillary 10a and the buffer bridge 42a. Referring now to Fig. 1A, a tee is placed between the outlet portion of the capillary 10a and the suppressor 18a. Backflow of this

30 flowing stream of buffer towards the inlet portion of the capillary can be prevented, e.g., by completely filling the reservoir 12a with buffer 11a and then sealing the reservoir 12a.

An electrical conductivity detector is preferred in the
invention. However, an electrical conductivity detector is
not critical in the invention. For example, a photometric
detector can be used. Other detectors that can be used
5   include a mass spectrometer, a refractive index detector
and a dielectric constant detector. Thus, any detector can
be used that detects ions better when the buffer is
suppressed.

10   The capillary of the invention can be negatively
charged, positively charged or neutral as discussed above.
If the capillary is positively charged and the ions of
interest comprise anions or if the capillary is negatively
charged and the ions of interest comprise cations, then
15 there can be ion exchange chromatography of the ions of
interest as well as electrophoresis of the ions of
interest. Usually, most of the separation of the invention
is believed to be due to electrophoresis. However, if the
capillary of the invention comprises an ion exchange
20 material (such as coating a capillary tube with an ion
exchange resin or packing a capillary tube with ion
exchange resin beads, a pellicular ion exchanger or a
microparticulate ion exchanger), then it is contemplated
that ion exchange chromatography can become an important
25 separation mode of the invention.

EXAMPLE 1A
        The system as generally shown in Fig. 1A is assembled.
The capillary 10a is a seventy five micrometer internal
30 diameter fused silica capillary sixty centimeters in
length. The tube 31a of Fig. 2A is five millimeters in
length and is made by stretching a heated and solvent
swollen NAFION™ tube to an internal diameter of one hundred
and twenty five micrometers. The electrode 36a is
35 positioned as shown in Fig. 2A since its polarity helps the

effectiveness of the suppressor 18a. The regenerant 20a is
five millimolar sulfuric acid flowing through the
suppressor 18a at a flow rate of one hundred microliters
per minute. The buffer 11a is one millimolar borax at a pH
5   of 8.4. Thus, the inside surface of the capillary 10a is
negatively charged The sample 16a contains ten milligrams
per liter each of monochloroacetate, dichloroacetate and
trichloroacetate. The sample is introduced into the
capillary 10a by dipping its end into the sample 16a,
10 lifting the reservoir 17a ten centimeters above the
reservoir 29a for thirty seconds, and then replacing the
capillary 10a back into the reservoir 12a. Twenty thousand
volts positive is applied to the electrode 14a. The wire
19a is grounded. A strip chart recorder is connected to
15 the conductivity detector 25a and it records a pherogram
showing a peak for trichloroacetate at about three point
nine minutes, a peak for dichloroacetate at about four
point one minutes and a peak for monochloroacetate at about
four point three minutes.
20

EXAMPLE 2A

    The experiment of Example 1A is repeated except that
the regenerant 20a is mere deionized water. The pherogram
shows a peak for monochloroacetate at about three point
25 nine minutes, a peak for dichloroacetate at about four
point one minutes and a peak for trichloroacetate at about
four point three minutes. This example shows that water
can be a source of regenerant hydrogen ions in the
invention.
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EXAMPLE 3A

    The system as generally shown in Fig. 1A is assembled.
The capillary 10a is a one hundred and fifty micrometer
internal diameter fused silica capillary forty centimeters
35 in length. The inside surface of the capillary 10a is made

to be positively charged by the following steps: (a) the
capillary is filled with a solution of: one percent
polyvinyl alcohol that is one hundred percent hydrolyzed;
two percent phosphoric acid; one percent poly diallyl
5   dimethyl ammonium chloride; and ninety six percent water;
(b) the capillary is placed in an oven at ninety degrees
centigrade for two hours; and (c) the capillary is cooled
and rinsed with buffer for one hour. The thickness of the
resulting modified polyvinyl alcohol coating in the
10 capillary is about one micrometer. The tube 31a of Fig. 2A
is five millimeters in length and is made by drilling a
block of solvent swollen NAFION™ and then letting it dry to
shrink down onto the capillary 10a and the tube 24a. The
internal diameter of the resulting channel through the
15 NAFION™ is about seventy micrometers. The electrode 36a is
positioned near the end of the NAFION™ block that is
connected to the capillary 10a so that its influence on the
effectiveness of the suppressor is minimized. The
regenerant 20a is five millimolar sulfuric acid flowing
20 through the suppressor 18a at a flow rate of one hundred
microliters per minute. The buffer 11a is one half
millimolar borax at a pH of 8.4. The sample 16a contains
ten milligrams per liter each of nitrite, nitrate, sulfate
and acetate. The sample is introduced into the capillary
25 10a by dipping its end into the sample 16a, lifting the
reservoir 17a ten centimeters above the reservoir 29a for
thirty seconds, and then replacing the capillary 10a back
into the reservoir 12a. Twenty thousand volts negative is
applied to the electrode 14a. The wire 19a is grounded. A
30 strip chart recorder is connected to the conductivity
detector 25a and it records a pherogram showing a peak for
sulfate at about four point five minutes, a peak for
nitrite at about five minutes, a peak for nitrate at about
five point three minutes and a peak for acetate at about
35 six minutes. The separation of nitrite and nitrite is

greater than expected from the electrophoretic mobilities of these two ions and is explained herein as probably being due to ion exchange chromatography in the capillary 10a.

Having described the preferred embodiments, it will be apparent to those skilled in the art that various modifications may be made to such embodiments and that such modifications are intended to be within the scope of the invention.

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1.   Apparatus for ion analysis comprising

     (a) ⁻capillary electrophoretic separating means for
separating ionic species comprising a capillary having
5   a first end in communication with a first electrolyte
reservoir containing first electrode means and a second
end having ion conduction means in communication with
a second electrolyte reservoir having second electrode
means, said first end of said capillary being capable
10   of receiving electrolyte from said first reservoir and
said ion conducting means at said second end of said
capillary being capable of conducting the current
generated between said first and said second electrodes
when an electrolyte is present in said capillary and
15   said first and said second reservoirs and a voltage is
applied to said electrodes,

     (b)   suppressor means for treating effluent eluted
from said capillary electrophoretic separating means,
said suppressor means including

20   (1) at   least   one   capillary   effluent
compartment means having an inlet end and an outlet end,
said inlet end being in communication with said second
end of said capillary,

             (2)   at least one regenerant compartment means
25   and

             (3)   at least one ion exchange membrane
partitioning said capillary effluent compartment means
and said regenerant compartment means, said ion exchange
membrane being preferentially permeable to the counter
30   ion of said ionic species, and

(c) detector means in communication with the outlet end of said suppressor means suitable for detecting resolved ionic species eluting therefrom.

2. The apparatus of Claim 1 wherein said detector
5 means comprise first and second spaced detection electrode means wherein at least one of said detection electrode means is in electrical communication with the effluent from said outlet end of said suppressor means.

3. The apparatus of Claim 2 wherein said detecting of
10 said resolved ionic species comprises measuring the conductivity of the effluent from said outlet end of said suppressor means.

4. The apparatus of Claim 1 wherein said capillary effluent compartment and said ion exchange membrane in
15 said suppressor means have substantially the same cross-sectional area.

5. The apparatus of Claim 4 wherein said capillary and said selective ion exchange membrane tube have a circular cross section of substantially the same
20 diameter.

6. The apparatus of Claim 1 wherein said ion conduction means comprises an amphoteric ion exchange membrane.

7. A method of ion analysis comprising

25   (a) passing a sample containing ionic species in an electrolyte solution, including transmembrane electrolyte ions of opposite charge to said ionic species, through capillary electrophoretic separating means in which said ionic species are separated and
30 wherein said capillary electrophoretic separating means

comprises a capillary having first and second ends
wherein said first end is in contact with a first
electrolyte reservoir containing electrolyte and first
electrode means and said second end comprises ionic
5   conduction means in communication with a second
electrolyte reservoir containing electrolyte and second
electrode means, said first and said second electrode
means having a voltage applied thereto to cause the
separation of said ionic species,

10   (b) flowing the effluent from the capillary
electrophoretic separating means through a suppressor
means having at least one capillary effluent compartment
means, at least one regenerant compartment means
containing regenerant and at least one ion exchange
15   membrane partitioning said capillary effluent and said
regenerant compartment means, said ion exchange membrane
being preferentially permeable to the counter ion of
said ionic species to allow said counter ion to cross
said membrane into said regenerant compartment means and
20   regenerant ions of the same charge to pass said membrane
into said effluent, and

              (c) flowing the treated effluent from the outlet
of said capillary effluent compartment in said
suppressor means through detection means in which said
25   separated ionic species are detected by measuring the
conductivity of said treated effluent.

8.   The method of Claim 7 wherein the voltage applied
to said first and said second electrode means is
sufficient to induce electroendosmotic flow through said
30· capillary.

9.   The method of Claim 8 wherein said
electroendosmotic flow is from said first end to said
second end of said capillary, the internal surface of

said capillary has a negative charge and said first electrode has a positive polarity as compared to said second electrode.

10. The method of Claim 8 wherein said electroendosmotic flow is from said first end to said second end of said capillary, the internal surface of said capillary has a positive charge and said first electrode has a negative polarity as compared to said second electrode.

11. In an improved capillary electrophoresis apparatus comprising a capillary, the capillary having a sample inlet portion and an outlet portion, a first electrode in electrical communication with the inlet portion of the capillary, a second electrode in electrical communication with the outlet portion of the capillary, a power supply in electrical communication with the first and second electrodes, wherein the improvement comprises: means for exchanging ions, the means for exchanging ions being in liquid communication with the capillary, the means for exchanging ions being stationary.

12. The apparatus of Claim 11, wherein the means for exchanging ions is a conduit, the conduit comprising an ion exchange material, the channel of the conduit being in liquid communication with the capillary.

13. The apparatus of Claim 12, wherein the second electrode is positioned near the exterior of the conduit.

14. The apparatus of Claim 11, further including means for detecting ions, the means for detecting ions being in liquid communication with the means for exchanging ions.

15. The apparatus of Claim 12, further including that the means for detecting ions is in liquid communication with the channel of the conduit.

16.   The apparatus of Claim 13, further including that the means for detection ions is in liquid communication with the channel of the conduit.

17.   In an improved capillary electrophoresis apparatus comprising a capillary, the capillary having a sample inlet portion and an outlet portion, a porous conduit means, the channel of the porous conduit means being in liquid communication with the capillary, a first electrode in electrical communication with the inlet portion of the capillary, a second electrode, the second electrode being in electrical communication with the porous conduit means, a power supply in electrical communication with the first and second electrodes, wherein the improvement comprises: means for exchanging ions, the means for exchanging ions being in liquid communication with the channel of the porous conduit means, the means for exchanging ions being stationary.

18.   The apparatus of Claim 17, wherein the means for exchanging ions is an ion exchange conduit, the ion exchange conduit comprising an ion exchange material, the channel of the ion exchange conduit being in liquid communication with the channel of the porous conduit.

19.   The apparatus of Claim 17, further including means for detecting ions, the means for detecting ions being in liquid communication with the means for exchanging ions.

20.   The apparatus of Claim 18, further including that the means for detecting ions is in liquid communication with the channel of the ion exchange conduit.

21.   An anion analysis method comprising the steps of:
(a) separating anions of interest by electrophoresis in a buffer solution;

(b) exchanging cations of the buffer for regenerant cations using a stationary means for exchanging cations thereby reducing the electrical conductivity of the buffer to produce a suppressed buffer;

(c) measuring the electrical conductivity of the suppressed buffer to determine the separated anions.

22. The method of Claim 21, wherein the buffer comprises a salt of a weak acid and the regenerant cations comprise hydrogen ions.

23. The method of Claim 21, wherein the buffer comprises a strong base and the regenerant cations comprise hydrogen ions.

24. A cation analysis method comprising the steps of:
(a) separating cations of interest by electrophoresis in a buffer solution;
(b) exchanging anions of the buffer for regenerant anions using a stationary means for exchanging anions thereby reducing the electrical conductivity of the buffer to produce a suppressed buffer;
(c) measuring the electrical conductivity of the suppressed buffer to determine the separated cations.

25. The method of Claim 24, wherein the buffer comprises a salt of a weak base and the regenerant anions comprise hydroxide ions.

26. The method of Claim 24, wherein the buffer comprises a strong acid and the regenerant anions comprise hydroxide ions.

27.   An anion analysis method comprising the steps of:

(a) introducing a sample into a capillary, the capillary containing an electrophoresis buffer, the sample comprising anions of interest, the electrophoresis buffer also being in contact with a cation exchange material, the cation exchange material partitioning the electrophoresis buffer from a source of regenerant cations;

(b) applying an electric field along the channel of the capillary so that the electrophoresis buffer flows towards the cation exchange material by electroosmotic flow;

(c) exchanging the cations of the electrophoresis buffer for regenerant cations with the cation exchange material whereby the electrical conductivity of the electrophoresis buffer is reduced to form a suppressed electrophoresis buffer;

(d) measuring the electrical conductivity of the suppressed buffer to determine the separated anions.

28.   The method of Claim 27, wherein in step (b) the electric field is applied along the channel of the capillary and across the cation exchange material.

29.   A cation analysis method comprising the steps of:

(a) introducing a sample into a capillary, the capillary containing an electrophoresis buffer, the sample comprising cations of interest, the electrophoresis buffer also being in contact with an anion exchange material, the anion exchange material partitioning the electrophoresis buffer from a source of regenerant anions;

(b) applying an electric field along the channel of the capillary so that the electrophoresis buffer flows towards the anion exchange material by electroosmotic flow;

(c) exchanging the anions of the electrophoresis buffer
for regenerant anions with the anion exchange material
whereby the electrical conductivity of the electrophoresis
buffer is reduced to form a suppressed electrophoresis
buffer;

(d) measuring the electrical conductivity of the
suppressed buffer to determine the separated cations.

30. The method of Claim 29, wherein in step (b) the
electric field is applied along the channel of the
capillary tube and across the anion exchange material.

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AMENDED CLAIMS

[received by the International Bureau on 4 February 1993 (04.02.93);
new claims 31-50 added; other claims unchanged (6 pages)]

31. A capillary electrophoresis apparatus comprising a
capillary, the capillary having a sample inlet portion and
an outlet portion, a first electrode in electrical
communication with the inlet portion of the capillary, a
second electrode in electrical communication with the
outlet portion of the capillary, a power supply in
electrical communication with the first and second
electrodes and a detector in liquid communication with the
outlet portion of the capillary characterized by means for
exchanging ions, the means for exchanging ions being in
liquid communication with the outlet portion of the
capillary and the detector, the means for exchanging ions
being stationary.

32. The apparatus of Claim 31, wherein the means for
exchanging ions is a conduit, the conduit comprising an ion
exchange material, the channel of the conduit being in
liquid communication with the outlet portion of the
capillary.

33. The apparatus of Claim 32 further characterized in
that the path of the electrical communication between the
first and second electrodes is across the conduit.

34. A capillary electrophoresis apparatus comprising a
capillary, the capillary having a sample inlet portion and
an outlet portion, a porous conduit, the channel of the
porous conduit being in liquid communication with the
outlet portion of the capillary, a first electrode in
electrical communication with the inlet portion of the
capillary, a second electrode, the second electrode being
in electrical communication with the outlet portion of the
capillary across the porous conduit, a power supply in
electrical communication with the first and second

electrodes and a detector in liquid communication with the
porous conduit characterized by means for exchanging ions,
the means for exchanging ions being in liquid communication
with the channel of the porous conduit and the detector,
the means for exchanging ions being stationary.

35. The apparatus of Claim 34, wherein the means for
exchanging ions is an ion exchange conduit, the ion
exchange conduit comprising an ion exchange material, the
channel of the ion exchange conduit being in liquid
communication with the channel of the porous conduit.

36. An anion analysis method comprising the steps of:
(a) separating anions of interest by electrophoresis in
a buffer solution;
(b) exchanging cations of the buffer for regenerant
cations using a stationary means for exchanging cations
thereby reducing the response of the buffer to a detector
to produce a suppressed buffer; and
(c) measuring the response of the suppressed buffer
with a detector to determine the separated anions.

37. The anion analysis method of Claim 36 wherein in
step (b) the electrical conductivity of the buffer is
reduced and in step (c) the electrical conductivity of the
suppressed buffer is measured.

38. A cation analysis method comprising the steps of:
(a) separating cations of interest by electrophoresis
in a buffer solution;
(b) exchanging anions of the buffer for regenerant
anions using a stationary means for exchanging anions
thereby reducing the response of the buffer to a detector
to produce a suppr ssed buffer; and

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(c) measuring the response of the suppressed buffer with a detector to determine the separated cations.

39.   The cation analysis method of Claim 8 wherein in step (b) the electrical conductivity of the buffer is reduced and in step (c) the electrical conductivity of the suppressed buffer is measured.

40.   An anion analysis method comprising the steps of:
(a) introducing a sample into a capillary, the capillary containing an electrophoresis buffer, the sample comprising anions of interest, the electrophoresis buffer also being in contact with a cation exchange material, the cation exchange material partitioning the electrophoresis buffer from a source of regenerant cations;
(b) applying an electric field along the channel of the capillary so that the electrophoresis buffer flows towards the cation exchange material by electroosmotic flow;
(c) exchanging the cations of the electrophoresis buffer for regenerant cations with the cation exchange material whereby the electrical conductivity of the electrophoresis buffer is reduced to form a suppressed electrophoresis buffer; and
(d) measuring the electrical conductivity of the suppressed buffer to determine the separated anions.

41.   The method of Claim 40, wherein in step (b) the electric field is applied along the channel of the capillary and across the cation exchange material.

42.   A cation analysis method comprising the steps of:
(a) introducing a sample into a capillary, the capillary containing an electrophoresis buffer, the sample comprising cations of interest, the electrophoresis buffer also being in contact with an anion exchange material, the

anion exchange material partitioning the electrophoresis
buffer from a source of regenerant anions;

(b) applying an electric field along the channel of the
capillary so that the electrophoresis buffer flows towards
the anion exchange material by electroosmotic flow;

(c) exchanging the anions of the electrophoresis buffer
for regenerant anions with the anion exchange material
whereby the electrical conductivity of the electrophoresis
buffer is reduced to form a suppressed electrophoresis
buffer; and

(d) measuring the electrical conductivity of the
suppressed buffer to determine the separated cations.

43. The method of Claim 42, wherein in step (b) the
electric field is applied along the channel of the
capillary tube and across the anion exchange material.

44. A capillary electrophoresis apparatus comprising a
capillary, the capillary having a sample inlet portion and
an outlet portion, a first electrode in electrical
communication with the inlet portion of the capillary, a
second electrode in electrical communication with the
outlet portion of the capillary, a power supply in
electrical communication with the first and second
electrodes and a detector in liquid communication with the
outlet portion of the capillary characterized by conduit
means for channeling flow of liquid from the outlet portion
of the capillary to the detector, the conduit means
comprising an ion exchange membrane means, the ion exchange
membrane means partitioning the outlet portion of the
capillary from an electrolyte holding space defined by a
means for holding an electrolyte.

45. The apparatus of Claim 44 further characterized in
that the path of the electrical communication between the
first and second electrodes is across the ion exchange
membrane means.

46. The apparatus of Claim 45 wherein the electrolyte
holding space contains an electrolyte in contact with the
ion exchange membrane means.

47. The apparatus of Claim 46 wherein the electrolyte
holding space contains a regenerant for regenerating the
ion exchange membrane means.

48. The apparatus of Claims 31-35 wherein the ion
exchange membrane means is capable of exchanging ions of an
electrophoresis buffer for regenerant ions thereby reducing
the detector response of the buffer to produce a suppressed
buffer.

49. A capillary electrophoresis apparatus comprising
generally an electrophoresis capillary, the capillary
defining an electrophoresis region adapted to contain a
buffer solution in which an electric field can be developed
by means of spaced electrodes connected to a power supply
to separate components of a sample introduced into the
electrophoresis region, a detector in liquid communication
with the bore of the capillary to detect sample components
separated in the electrophoresis region, the apparatus
being characterized by ion exchange means for exchanging
ions of the buffer solution for regenerant ions thereby
reducing the detector response of the buffer solution to
produce a suppressed buffer solution, the ion exchange
means comprising an ion exchange membrane which forms a
partition between the bore of the capillary and a

regenerant space defined by a means for holding a regenerant.

50. The apparatus of Claim 49 further characterized in that the path of the electrical communication between the electrodes is across the ion exchange membrane.

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 G01N27/447

II. FIELDS SEARCHED

Minimum Documentation Searched[7]	
Classification System	Classification Symbols
Int.Cl. 5	G01N

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

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A	US,A,4 908 116 (R. N. ZARE) 13 March 1990 see abstract; figure 1	1
A	EP,A,0 295 942 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 21 December 1988 see abstract; figure 3	1
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° Special categories of cited documents :[10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the International filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
14 DECEMBER 1992	23. 12. 92
International Searching Authority	Signature of Authorized Officer
EUROPEAN PATENT OFFICE	DUCHATELLIER M.

III. DOCUMENTS CONSIDERED TO BE RELEVANT	(CONTINUED FROM THE SECOND SHEET)	
Category*	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
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A	EP,A,0 069 285 (BIOTRONIK) 12 January 1983 cited in the application see abstract & US,A,4 459 357 (K. H. JANSEN) 10 July 1984 ---	1
A	EP,A,0 075 371 (THE DOW CHEMICAL CO.) 30 March 1983 cited in the application see abstract & US,A,4 751 004 (T. S. STEVENS) 14 June 1988 -----	1

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The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 14/12/92

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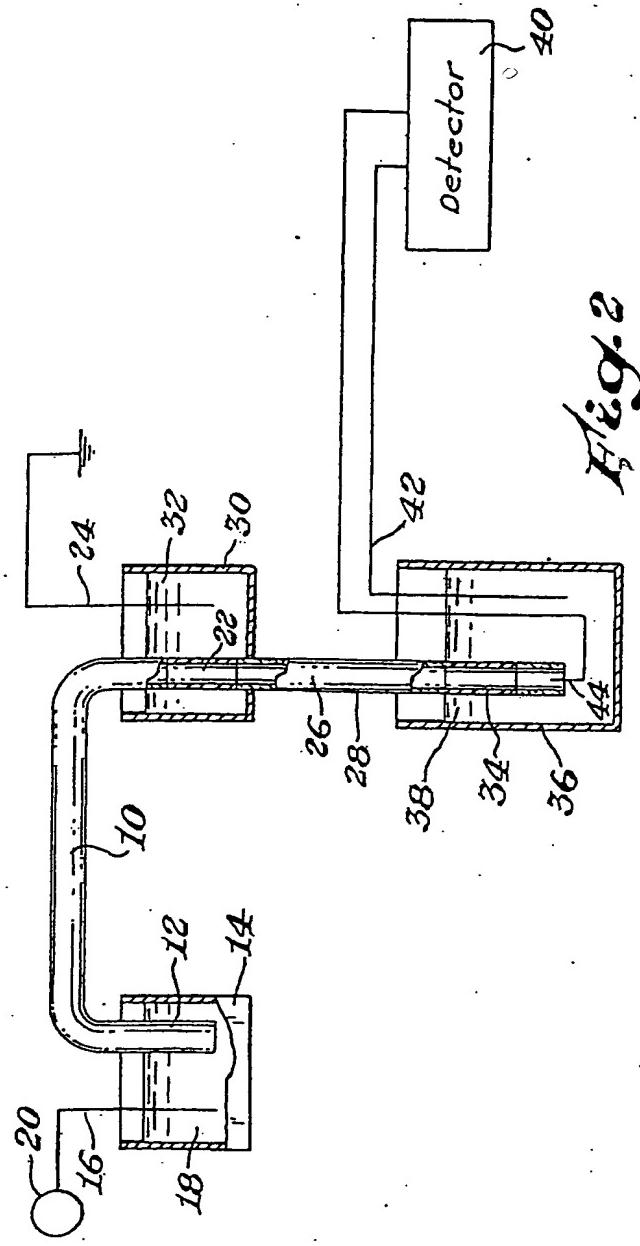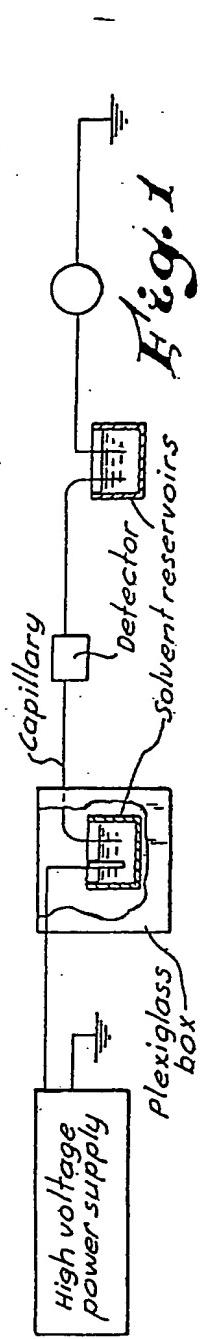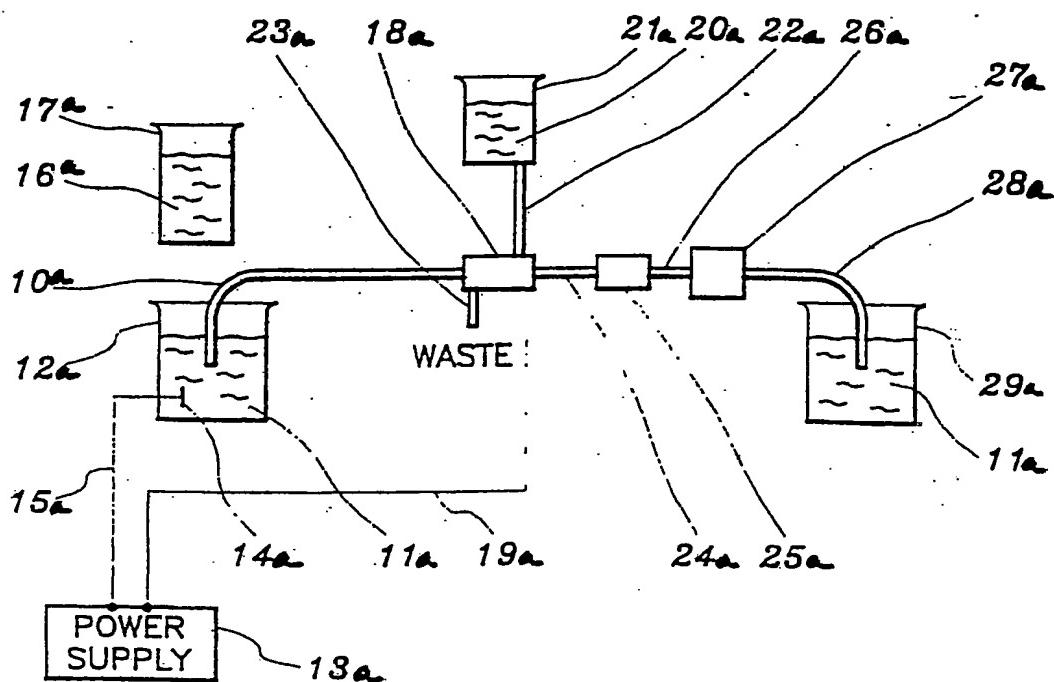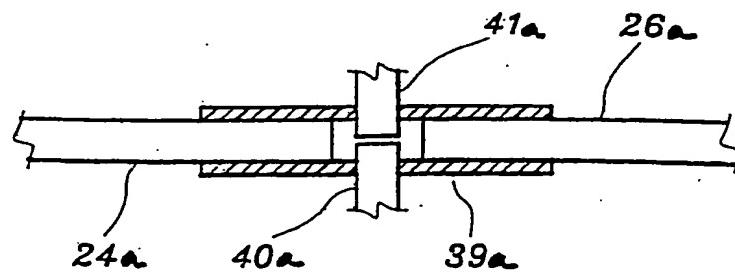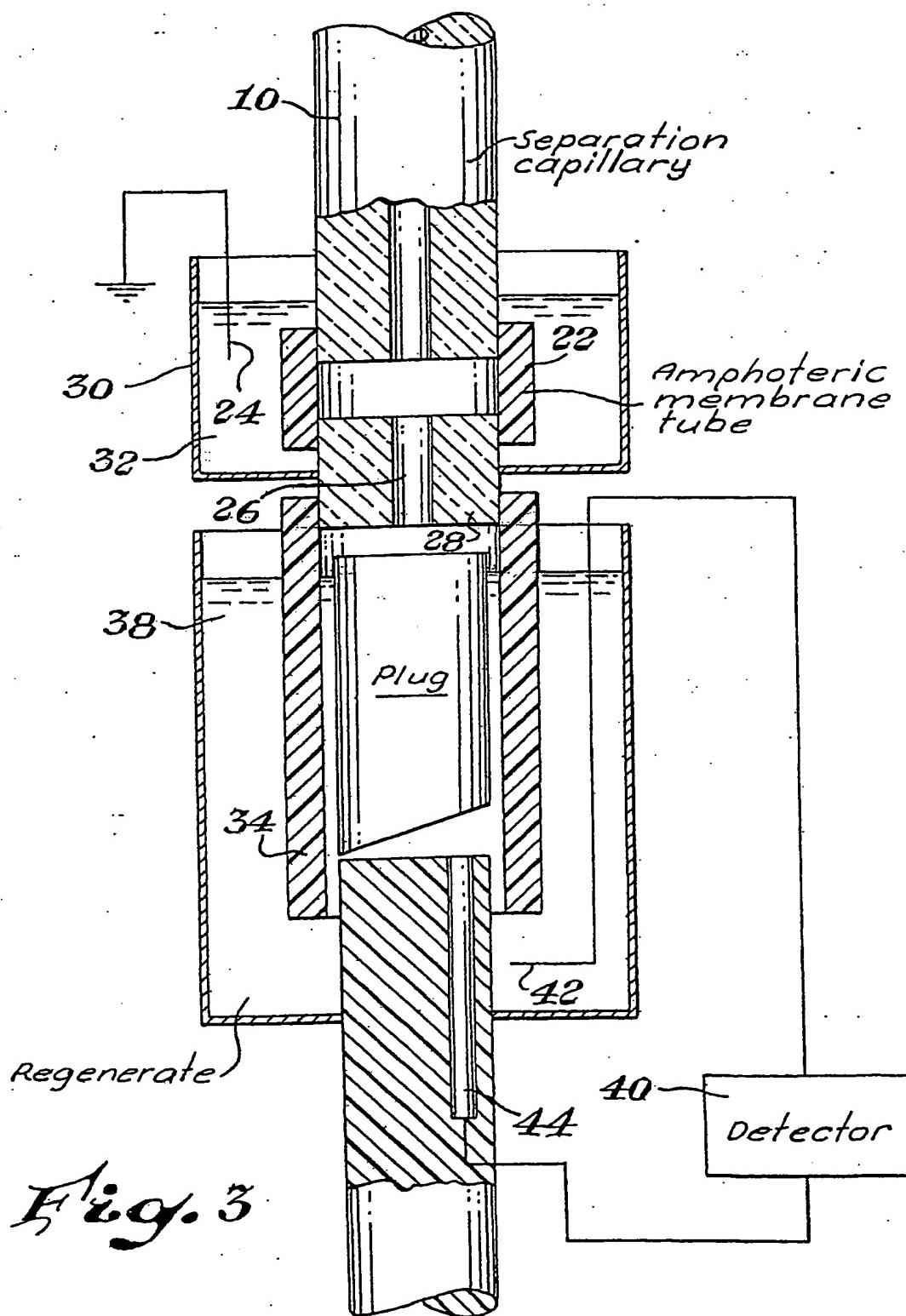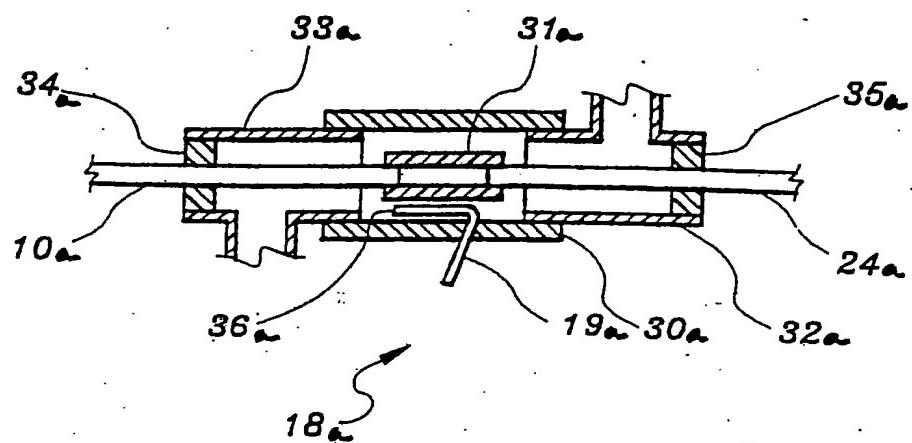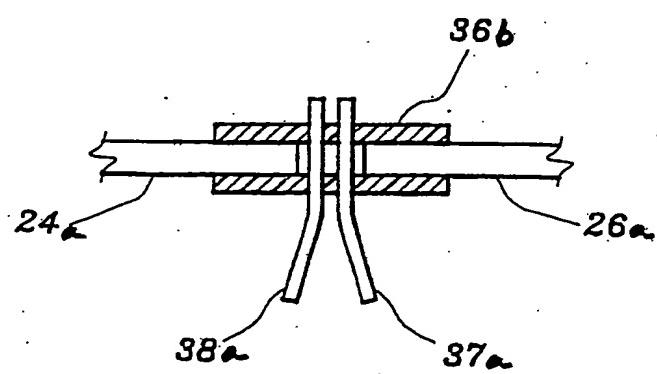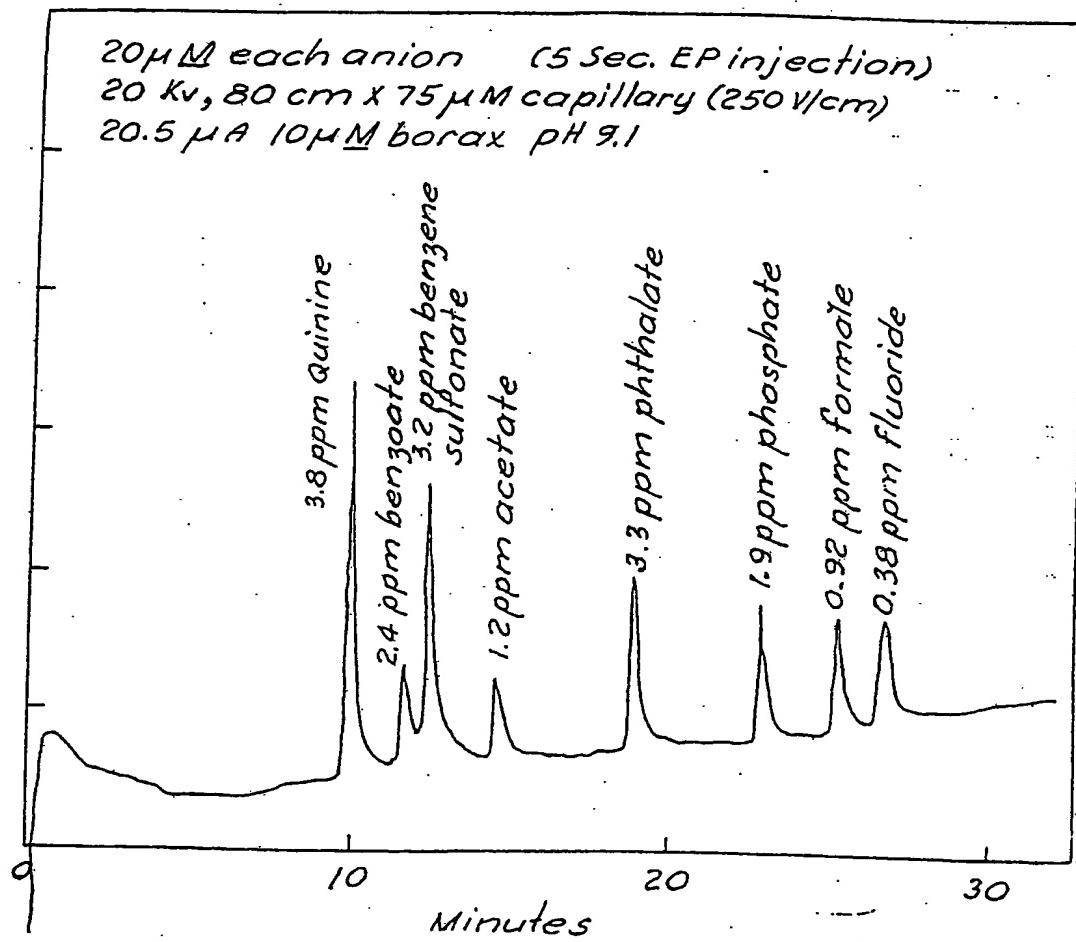
EPO FORM P0479

Fig. 1

Fig. 2

FIG. 1A

FIG. 4A

10 — separation capillary

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22 — Amphoteric membrane tube

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Plug

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Regenerate

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40 — Detector

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Fig. 3

FIG. 2A

FIG. 3A

20 μ M each anion   (5 Sec. EP injection)
20 Kv, 80 cm x 75 μM capillary (250 V/cm)
20.5 μA 10μM borax pH 9.1

3.8 ppm Quinine
2.4 ppm benzoate
3.2 ppm benzene sulfonate
1.2 ppm acetate
3.3 ppm phthalate
1.9 ppm phosphate
0.92 ppm formate
0.38 ppm fluoride

Minutes

Fig. 4

5 / 6

★ **DOWC**   X25   93-117725/14   ★ **WO 9306475-A1**
**Capillary electrophoretic appts. - includes ion exchange membrane
connected to downstream end of capillary preferentially permeable
to counterion of sepd. ionic species (Eng)**
   DOW CHEM CO 91.10.04 91US-771597 (91.09.24 91US-764645)
   J04 (93.04.01) G01N 27/447
92.09.23 92WO-US08071 N(AT AU BB BG BR CA CH CS DE DK ES FI
GB HU JP KR LK LU MG MN MW NL NO PL RO RU SD SE) R(AT
BE CH DE DK ES FR GB GR IE IT LU MC NL OA SE)
Addnl. Data: 91.10.04 91US-771336
Appts. includes a capillary with a sample inlet and an outlet. A first
electrode is in electrical communication with the inlet and a second
electrode in communication with the outlet. The first and second
electrodes are connected to a power supply. The appts. also includes
a stationary ion exchanger in liq. communication with the capillary.
     Cations of interest are pref. sepd. by electrophoresis in a buffer
soln.. The anions of the buffer are exchanged for regenerant anions
using a stationary ion exchanger to reduce the electrical
conductivity of the buffer producing a suppressed buffer. The
electrical conductivity of the suppressed buffer is measured to
determine the sepd. cations.
     ADVANTAGE - The appts. increases the sensitivity of
detection of ionic species sepd. by capillary electrophoresis. (63pp
Dwg.No.1a/6)
   CT: 1.Jnl.Ref EP180321 EP295942 EP69285 EP75371 US4459357
   US4751004 US4908116 US4999098
N93-089687   X25-H09 X25-R01C